We claim:

1. A recombinant DNA sequence which encodes the complete amino acid sequence of a glutamine synthetase (GS).

2. The recombinant DNA sequence of claim 1, which encodes the complete amino acid sequence of an eukaryotic GS.

3. The recombinant DNA sequence of claim 2, which encodes the complete amino acid sequence of a mammalian GS.

4. The recombinant DNA sequence of claim 3, which encodes the complete amino acid sequence of a rodent GS.

5. The recombinant DNA sequence of claim 4, which encodes the complete amino acid sequence of a hamster GS.

6. The recombinant DNA sequence of claim 5, which comprises the amino acid coding portion of the sequence shown in Figure 2.

7. The recombinant DNA sequence shown in Figure 2.

8. A recombinant DNA sequence from one species which hybridises under high stringency conditions with the recombinant DNA sequence of any one of claims 1 to 6 or a part thereof from a different species.

9. The recombinant DNA sequence of any one of claims 1 to 8, which is cDNA.

10. The recombinant DNA sequence of claim 9 wherein the cDNA is derived by reverse transcription.

11. The recombinant DNA sequence of any one of claims 1 to 10, which comprises a fragment of genomic DNA.

12. Use of the recombinant DNA sequence of any one of claims 1 to 6 or any fragment thereof as a hybridisation probe.

13. The recombinant DNA sequence of any one of claims 1 to 11 for use in medical or diagnostic methods such as for detecting disease states in which the level of GS in a subject is altered.

14. A recombinant DNA vector comprising the recombinant DNA sequence of any one of claims 1 to 11.

15. The vector of claim 14, which is an expression vector capable, in a transformant host cell, of expressing the recombinant DNA sequence of any one of claims 1 to 11.

16. The vector of claim 14, further comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS

17. The vector of claim 15, further comprising a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS, the vector also being capable, in a transformant host cell, of expressing the recombinant DNA sequence for the desired protein.

18. The vector of claim 15 or claim 17, wherein the GS-encoding recombinant DNA sequence is under the control of a regulatable promoter.

19. The vector of claim 18, wherein the regulatable promoter is a heat shock promoter or a metallothionein promoter.

20. Plasmid pSVLGS.1.

21. Plasmid pSV2.GS.

22. Plasmid pZIPGS.

23. Plasmid pSVLGS.tPA16

24. Plasmid pSVLGS.tPA17

25. A host cell transformed with a vector according to any one of claims 14 to 24.

26. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS, which comprises co-transforming a host cell with a vector according to claim 15, claim 18 or claim 19 when dependent on claim 15, or any one of claims 20 to 22, and a vector comprising said desired protein recombinant DNA sequence.

27. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS which comprises transforming a host cell with a vector according to claim 17, claim 18 or claim 19 when dependent on claim 17, claim 23 or claim 24.

28. The method of claim 26 or Claim 27, wherein the desired protein is tissue plasminogen activator.

29. The method of any one of claims 26 to 28, wherein amplification is achieved by selection for resistance to progressively increased levels of a GS inhibitor.

30. The method of claim 29, wherein the GS inhibitor is phosphinothricin or methionine sulphoximine.

31. The method of claim 29 or claim 30, wherein after amplification, the level of GS accumulation is reduced by adding glutamine to the culture medium.

32. The method of any one of claims 29 to 31, wherein the amount of GS inhibitor required

to cause amplification is reduced by the addition of methionine to the culture medium.

33. The method of any one of claims 26 to 30 when dependent on claim 18 or claim 19, wherein the GS-encoding recombinant DNA sequence expression is switched on during selection and amplification and subsequently down-regulated.

34. Use of a vector according to any one of claims 15 and 17 to 24 as a dominant selectable marker by transforming a host cell which contains an active GS gene with the vector, thereby conferring transformant cells with resistance to GS inhibitors.

35. Use of a vector according to any one of claims 15 and 17 to 24 in endowing a cell line with the ability to survive in a medium lacking glutamine by transforming a host cell either completely lacking or reduced in GS activity with the vector.

36. The method of any one of claims 26 to 34, wherein the host cell is a mammalian cell.

37. The method of any one of claims 26 to 34, wherein the host cell is a CHO-KI cell.

38. The method of claim 35, wherein the host cell is a myeloma cell.

add β1

as amended by ECN 4-30-92

ABSTRACT OF THE DISCLOSURE

Recombinant DNA sequences which encode the complete amino acid sequence of a glutamine synthetase, vectors containing such sequences, and methods for their use, in particular as dominant selectable markers, for use in co-amplification of non-selected genes and in transforming host cell lines to glutamine independence.